

REMARKS

Claims 28-39 and 48-54 are pending. Claims 40-47 are withdrawn from consideration. The Examiner has mistakenly identified claims 34 and 54 as withdrawn from consideration. Claims 34 and 54, both depend indirectly from claim 28, and are linked to the invention by claim 28. Both claims were also previously examined by the prior Examiner on the merits. Appropriate correction by the Examiner is requested to properly list claims 34 and 54 as pending.

Claims 28, 50-53 and 55 are amended, as discussed below.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 28-33, 35-39, 48-53 and 55 under 35 U.S.C. 112 (Written Description)

Claims 28-33, 35-39, 48-53 and 55 are rejected under 35 U.S.C. 112, as lacking written description. The Examiner contends:

1. The specification and claims do not provide any guidance as to what structural feature all of the catalyst would share, and it is not possible to determine which compounds the catalyst libraries would encompass or the product of the catalytic reaction because there is no common structural attributes;
2. The specification and claims do not describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof;
3. The specification does not provide any guidance as to which catalyst can have a reversible reaction, and it is not possible to determine which catalysts have a reversible catalytic reaction.

This rejection is respectfully traversed. Foremost, Applicants do not agree that the presence of a common structural feature or element unifying all catalysts or product produced by the catalytic reaction is necessary to practice the claimed method. Applicants are not claiming catalysts molecules or products of catalyst reactions, rather Applicants are claiming methods for identifying a catalyst of interest.

In this regard, the Examiner has not explained, and it is not apparent how the claimed method requires that catalysts or products of the catalyst reactions have a common unifying structural feature in order for the artisan to practice the claimed invention, as none of the steps

require a particular structural or functional attribute of the catalyst, other than as part of a catalyst-substrate or catalyst-product unit. See, e.g., Claim 28:

28. A method for identifying a catalyst of interest from a library of catalysts, said method comprising:

- a) providing a library of catalysts comprising at least two different units, wherein each of said units comprises a catalyst attached to at least one substrate, each unit having the structure catalyst-substrate, wherein said catalyst is attached to said at least one substrate in a manner that allows a catalytic reaction to occur between said catalyst and said at least one substrate;
- b) providing conditions suitable for said catalyst to catalyze the reaction of said at least one substrate to form one or more products, wherein at least one product of said catalytic reaction remains attached to said catalyst;
- c) providing at least one reagent or condition which converts said at least one attached product to at least one substrate so as to regenerate said catalyst-substrate units;
- d) repeating said b) and c) at least once; and
- e) selecting said catalyst with the desired catalytic activity.

The specification also clearly establishes that a common unifying structural feature is not required to practice the claimed invention. Indeed, as disclosed in the specification, the invention is applicable to catalysts in general, including organic and inorganic catalysts, protein, enzymes, peptides, nucleic acids, biopolymers and non-biological catalysts, e.g., small molecules. See the specification, e.g., at, page 27, lines 26-32. The specification also provides examples for protein and nucleic acid catalysts (see, e.g., Examples 1-9). The specification further provides specific examples for synthetic catalysts. In particular, Example 5 and Figure 10 show a synthetically prepared peptide which is akin to a chemical catalyst, and accordingly a synthetic combinatorial library. Thus, the specification provides both a disclosure and examples for the major categories of catalysts: (1) peptide/protein catalysts, (2) nucleic acid catalysts and (3) synthetic catalysts. Applicants have clearly demonstrated that the claimed invention is not limited to a particular type of catalyst or to a catalyst having a particular structure or function, as is asserted by the Examiner.

Notwithstanding that neither the claims nor the specification support the allegation that a common structural attribute is required, the Examiner has also not given any reason why a common structural feature of the catalysts is relevant to the claimed method, and more particularly, why a common structural feature of the catalyst is relevant to the determination of the whether the written description requirement has been satisfied. If the Examiner maintains this

rejection, which would be plainly improper, Applicants respectfully request the Examiner to provide a basis as to why the disclosure of a common structural element for a catalysts is relevant to the claimed invention, and more particularly, why such disclosure is relevant to the issue of whether Applicants have described the claimed method in sufficient detail such that one skilled in the art can conclude that the inventors had possession of the claimed invention. See *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

The Examiner also alleges that the specification and claims do not provide "any guidance" as to which catalyst can have a reversible catalytic reaction, and it is not possible to determine which catalyst will have a reversible catalytic reaction. This Examiner's conclusion is clearly not correct as Applicants have provided both general and specific guidance to the artisan on this very issue. In this regard, the Examiner is referred to the specification at page 20 to page 22 and to Figure 3, which provides both general guidance and specific examples of the considerations an artisan would need to undertake for establishing a reversible catalytic reaction. For example, the specification discloses that for the direct substrate reloading process, the reaction is preferably energetically favorable. The specification also discloses the advantage of the reversible reaction from product to substrate following a different path from the reaction of substrate to product, as shown, e.g., in Figure 3. Moreover, many examples are provided, including the isomerization of a compound, in which the reverse reaction is favored, and in which the buffer should contain a reactant that, together with the product, is at a higher energy than the substrate. An example involving two substrates is also provided, namely, the RNA polymerization catalytic reaction in which the first substrate is a 3'-hydroxyl group on a ribonucleotide and the second substrate are various ribonucleoside-triphosphates. Although the forward reaction is driven by hydrolysis of the ribonucleoside-triphosphates and is favored, the specification teaches that the reverse regeneration involving hydrolysis of the phosphodiester bond can be promoted by addition of a ribonuclease. The specification further teaches that although in some cases it would clearly be preferred to use another enzyme to regenerate a substrate, an artisan can use non-enzymatic reagents to regenerate the substrate, including for example, pH conditions, temperature, chemicals, and spontaneous isomerization. For example, the specification discloses (at page 20) the use of non-enzymatic reagents including "nucleophile" and "1-3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) and alcohol" for studying the desired reaction of "ester hydrolysis." Regeneration of the substrate without an enzyme by spontaneous isomerization is also illustrated in Figure 3, which is described in the specification on pages 21-24, and in particular, Figure 3D, in which the regeneration of substrate (i.e., converting product to substrate)

is energetically favored.

Other examples are given in the specification (on page 19) and include the reaction and appropriate reagents to obtain a reversible reaction: (1) "DNA polymerization" and a "DNase"; (2) "RNA polymerization" and an "RNase"; (3) "RNA polymerization using nucleotides containing unnatural bases" and "RNA backbone cleaving enzyme"; (4) "Glycogen degradation" and "UDP-glucose + glycogen synthase"; (5) "Polysaccharide synthesis" and "Polysaccharide cleaving enzyme"; (6) "Sequence specific dsDNA cleavage" and "Sequenase + deoxyribonucleoside-triphosphates"; (7) "Ester hydrolysis" and "activated nucleophile"; (8) "Amid bond formation" and "protease"; (9) "Lipid hydrolysis" and "acetylCoA + lipid synthase"; (10) "phosphorylation" and "phosphatase"; (11) "Ester hydrolysis" and "1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) + alcohol"; (12) "D-to-L form isomerization" and "L-to-D isomerase"; (13) "Proline trans-to-cis isomerization" and "Proline cis-to-trans isomerase"; (14) "Lactone or lactam cyclization" and "Lactonase or Lactamase"; (15) "Oxidation or reduction", "Reductase or Oxidase"; and (16) "Desulfotation", "Sulfotransferase".

Thus, the Examiner's assertion that Applicants have not provided "any guidance" is plainly incorrect. Moreover, as is clear from the above, Applicants have provided very detailed guidance such that an artisan would readily conclude that Applicants were in possession of the claimed invention as Applicants have provide a detailed disclosure sufficient to show that they were in possession of the invention as claimed.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 28-33, 35-39, 48-53 and 55 under 35 U.S.C. 112 (Enablement)

Claims 28-33, 35-39, 48-53 and 55 are rejected under 35 U.S.C. 112 as allegedly lacking enablement.

The basis for the enablement rejection is summarized by the Examiner on page 10-12 of the Office action, as follows:

- a. The specification fails to give adequate direction and guidance to perform the method for identifying a catalyst of interest from a library of catalysts, as (1) the catalyst has an "unknown" core structure, the specification does not provide any guidance for the type of condition in which the catalyst converts the substrate into product; (2) each catalyst would require a different "condition" to form a product; (3) cross-reactions can occur

with a mixture of catalyst, (4) the specification does not provide any guidance as to the type of condition in which product is converted back to substrate and each product would required a different condition in order to convert the product back to the substrate, (5) the type of substrate is unknown because "is the substrate the same as the original substrate or different"; (6) the specification does not provide any guidance as to selecting the catalyst with the desired catalyst of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst.

- b. [mistakenly labeled c]. "The breadth of the claims is open-ended regarding the type of catalyst; the type of product produce [sic] in the forward reaction; the type of substrate produce [sic] in the reverse reaction: condition for the forward; and condition for the reverse."
- c. [mistakenly labeled d] The state of the prior art at the time of the invention was made is such that each type of catalyst requires different reaction conditions (e.g., catalytic activity) and produces different product. In general the synthesis of libraries of catalysts do not have standard method and testing for their reactivities are known to be difficult."
- d. [mistakenly labeled e] The art is inherently unpredictable because each type of catalyst has different catalytic activity and to select the catalyst with the desired catalytic activity of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst.

This rejection is respectfully traversed.

The Examiner contends that Applicants have failed to provide guidance for identifying a catalyst having an "unknown" core structure. It is not clear what the examiner means by this statement. The invention is directed to methods for identifying catalysts, Applicants are not claiming catalysts per se. Moreover, as discussed in regard to the written description rejection, the claimed methods are not limited to a single type of catalysts (e.g., only protein, only protease, etc.). Indeed, as disclosed in the specification, the invention is applicable to catalysts in general, including organic and inorganic catalysts, protein, enzymes, peptides, nucleic acids, biopolymers and non-biological catalysts, e.g., small molecules. See the specification, e.g., at, page 27, lines 26-32. The specification also provides examples for protein and nucleic acid catalysts (see, e.g., Examples 1-4 and 6-9). The specification further provides specific examples for synthetic catalysts. In particular, Example 5 and Figure 10 show a synthetically prepared peptide which is akin to a chemical catalyst, and accordingly a synthetic combinatorial library. Thus, the

specification provides both a disclosure and examples for the major categories of catalysts: (1) peptide/protein catalysts, (2) nucleic acid catalysts and (3) synthetic catalysts. Applicants have clearly demonstrated that the claimed invention is not limited to a particular type of catalyst or to a catalyst having a particular structure or function, as is asserted by the Examiner.

The Examiner also contends that the specification does not provide "any guidance" for the type of condition in which the catalyst converts the substrate into product. This assertion is plainly incorrect. Applicants have provided a detailed disclosure such that one skilled in the art would be able to practice the invention to many diverse types of catalysts, including protein, nucleic acid and synthetic catalysts, the major catalyst types. In this regard, the specification provides a detailed disclosure and examples of how to practice the claimed invention for many different types of protein and nucleic acid catalysts. Applicants respectfully direct the Examiner to the specification at page 20 to page 22, the Figures and Examples 1-9, which provides both general guidance and specific guidance for establishing a reversible catalytic reaction for many types of catalyst. Applicants also disclose specific details and guidance for catalysts in the reactions of DNA polymerization; RNA polymerization; glycogen degradation, polysaccharide synthesis, sequence specific dsDNA cleavage, ester hydrolysis, lipid hydrolysis; isomerization; lactone or lactam cyclization, oxidation or reduction, and desulfotation.

In addition to the protein and nucleic acid catalysts, which are addressed in detail in throughout specification, the specification also provides guidance for the applicability of the claimed invention to a synthetic catalyst. As discussed at the interview with the prior Examiner, the specification provides an example for small synthesized catalysts. In particular, Example 5 (Figure 10) of the specification was specifically provided to show the applicability of the claimed invention in the field of synthetic combinatorial chemistry. Although the catalyst itself is a peptide, the peptide was synthesized. Accordingly, this example further demonstrates that difference between categories of catalyst (e.g., protein, nucleic acid and synthetic) is not a barrier to carrying out the claimed invention.

Moreover, as also discussed in the interview with the prior Examiner, and as summarized in the prior response, enzymatic catalyst, have a very fast turnover rate compared to other catalysts and a relatively complex three-dimensional structure, and can accordingly be considered to be as complex as or even more complex than other catalysts. That is, a non-enzymatic or non-nucleic acid catalysts (such as, chemical catalysts) are certainly not *per se* more difficult to employ in the claimed invention than a protein or nucleic acid catalysts, and the

embodiments illustrative of the protein and nucleic acid catalysts, including the difficult enzymatic catalysts, sufficiently represent the broad applicability of the claimed invention.

Furthermore, although there are some specific considerations which are relevant to the specific catalyst employed for use in the claimed invention (e.g., selecting an appropriate substrate and connecting the catalyst and substrate), any such specific considerations would be well within the ability of the highly skilled artisan applicable to this art and would entail only routine experimentation. In this regard, the Examiner's rejection clearly implies that routine experimentation is not permitted. However, it is now well-established that enablement is not precluded by the necessity for routine experimentation. See *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Indeed, any assertion that the specification must teach a skilled artisan how to predict the sufficiency of each catalyst-substrate unit suitable for use in the present invention prior to actually producing and testing is improper because it precludes the availability and necessity for routine testing. See *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (noting that enablement is not precluded by the necessity for some experimentation such as routine screening.) Indeed, even if experimentation might be time consuming, it is the nature and not the amount of experimentation that is determinative of non-enablement. Although some experimentation would be required to apply the invention to some catalysts and substrates, the experimentation would not be considered by an artisan to be undue.

The Examiner also asserts that each catalyst would require a different "condition" to form a product. This is also clearly incorrect. Indeed, in preferred embodiments, the invention may be applied under identical conditions. For example, when assessing a library of proteases (i.e., different protease), identical conditions are preferably employed to form a product for each catalysts, so as to assess which catalysts performs the best under the identical conditions.

This rejection is also seemingly opposite to a rejection asserted by the prior Examiner, namely, that the assertion that the claims were limited to the situation in which all of the catalysts catalyze the same reaction and that all of the substrates react to form the same product. See the Office Action of April 23, 2002. In response, Applicants explained that the claims are not limited to the same catalytic reaction. Indeed, the claimed method is applicable to both catalysts that have the same or closely related catalytic activities (such as, a variant protease library) or to catalysts that have different catalytic activities. (See, e.g., original claims 9 and 10.)

The Examiner also asserts that enablement is precluded due to the possible cross-reaction resulting with a mixture of catalyst. Applicants respectfully disagree and direct the Examiner to the specification at page 42, where one solution to avoiding cross-reactivity is

disclosed, for example, by covalently linking the substrate to ensure no cross reactivity. The Examiner attention is also directed to the specification at page 48, which discloses enzyme dependent cleavage of phage from a solid support, and in which the inventors specifically concluded that cross-reactivity did not appear to be significant even with a very active enzyme like SNase. Thus, the Examiner's assertion that cross-reactivity precludes enablement of the claimed invention is clearly not correct and is rebutted by the above-evidence.

The Examiner's assertion that the specification does not provide "any guidance" as to the type of condition in which product is converted back to substrate is also improper. As previously discussed, the specification provides both general and specific guidance as to proper condition for converting product back to substrate. For example, Applicants respectfully direct the Examiner to the specification at page 20 to page 22 and to Figure 3, which provides both general guidance and specific examples of the considerations an artisan would need to undertake for establishing a reversible catalytic reaction. As disclosed in the specification, for the direct substrate reloading process, the reaction is preferably energetically favorable. The specification also discloses the advantage of the reversible reaction from product to substrate following a different path from the reaction of substrate to product, as shown, e.g., in Figure 3. Furthermore, many examples are provided, including the isomerization of a compound, in which the reverse reaction is favored, and in which the buffer should contain a reactant that, together with the product, is at a higher energy than the substrate. An example involving two substrates is the RNA polymerization catalytic reaction, in which the first substrate is a 3'-hydroxyl group on a ribonucleotide and the second substrate are various ribonucleoside-triphosphates. Although the forward reaction is driven by hydrolysis of the ribonucleoside-triphosphates and is favored, the specification teaches that the reverse regeneration involving hydrolysis of the phosphodiester bond can be promoted by addition of a ribonuclease. The specification also discloses that although in some cases it would clearly be preferred to use another enzyme to regenerate a substrate, an artisan can also use non-enzymatic reagents to regenerate the substrate, including for example, pH conditions, temperature, chemicals, and spontaneous isomerization. For example, the specification discloses (at page 20) the use of non-enzymatic reagents including "nucleophile" and "1-3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) and alcohol" for studying the desired reaction of "ester hydrolysis." Regeneration of the substrate without an enzyme by spontaneous isomerization is also illustrated in Figure 3, which is described in the specification on pages 21-24, and in particular, Figure 3D, in which the regeneration of substrate (i.e., converting product to substrate) is energetically favored.

Again, other examples are given in the specification (on page 19) are: (1). "DNA polymerization" and a "DNase"; (2) "RNA polymerization" and an "RNase"; (3) "RNA polymerization using nucleotides containing unnatural bases" and "RNA backbone cleaving enzyme"; (4) "Glycogen degradation" and "UDP-glucose + glycogen synthase"; (5) "Polysaccharide synthesis" and "Polysaccharide cleaving enzyme"; (6) "Sequence specific dsDNA cleavage" and "Sequenase + deoxyribonucleoside-triphosphates"; (7) "Ester hydrolysis" and "activated nucleophile"; (8) "Amid bond formation" and "protease"; (9) "Lipid hydrolysis" and "acetylCoA + lipid synthase"; (10) "phosphorylation" and "phosphatase"; (11) "Ester hydrolysis" and "1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) + alcohol"; (12) "D-to-L form isomerization" and "L-to-D isomerase"; (13) "Proline trans-to-cis isomerization" and "Proline cis-to-trans isomerase"; (14) "Lactone or lactam cyclization" and "Lactonase or Lactamase"; (15) "Oxidation or reduction", "Reductase or Oxidase"; and (16) "Desulfotation", "Sulfotransferase".

Thus, the Examiner's assertion that Applicants have not provided "any" guidance is clearly not correct. Moreover, as is clear from the above, Applicants have provided detailed guidance such that an artisan is enabled to practice the claimed invention. Any implication that the specification must provide very specific details of how to obtain a reversible reaction in every case is also improper because it precludes the availability and necessity for routine testing. See *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (noting that enablement is not precluded by the necessity for some experimentation such as routine screening.)

The Examiner also asserts that the type of substrate is unknown and ponders: "is the substrate the same as the original substrate or different". The claims clearly recite providing a reagent or condition to form a product that remains attached to the catalyst and then providing a reagent or condition that converts the attached product back to the substrate so as to regenerate the catalysts-substrate units. In this regard, the invention allows the artisan to assess the suitability of a catalyst based on multiple catalytic activities (substrate to product catalytic turnovers).

The Examiner further asserts that the specification does not provide "any guidance" as to selecting the catalyst with the desired catalyst of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst. Contrary to this assertion, the specification provides detailed guidance for how a catalyst of interest can be selected. For example, the catalyst of interest can be selected based on how fast or slow it catalyzes a reaction by using a binding column. See, e.g., the specification at page 10, line 14 to page 13, line 22. As discussed

in the specification, one method of selecting a catalyst of interest is by using a product binding column, wherein a receptor that binds the product is coupled to the matrix of the column. In addition to the use of a product binding column, the specification also teaches selection of a catalyst of interest using a substrate binding column, selection of a catalyst of interest by virtue of cleavage from a support, and selection of a catalyst of interest by virtue of attachment to a support, e.g., upon reaction. See the specification on page 33, line 4 to page 35, line 8.

As further discussed in the specification, the present invention permits an artisan to determine even minor differences between catalysts, based on multiple catalytic activity turnovers. In this regard, Example 2 provides a protocol for how a catalyst of interest can be selected from a mixture of catalysts. As described in Example, 2, enzymes with glucosidase activity can be selected, for example, by displaying/attaching enzymes with glucosidase activity and the substrate, a glycogen linker, on the surface of a filamentous phage, as described in Example 1. The enzymes are also attached to a column through the glycogen linker. Enzymes with desired activity will cleave the bond between the two sugars, releasing the phage with a glucose unit attached to it. However, glycogen synthase present in the buffer will catalyze condensation of glucose and UDP-glucose, and as a result, reattach the enzyme to column through a portion of the glycogen. Enzymes having the highest catalytic efficiency will flow through the column the fastest, and can be collected from the first column fractions. Example 8 also provides a protocol for selecting RNases of interest.

Thus, the assertion that the specification does not provide "any guidance" as to selecting the catalyst with the desired catalyst of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalysts clearly is not correct.

The Examiner also contends that the "breadth of the claims is open-ended regarding the type of catalyst; the type of product produce [sic] in the forward reaction; the type of substrate produce [sic] in the reverse reaction; condition for the forward; and condition for the reverse."

However, as explained above, the present method is applicable to catalysts in general, and the specification provides detailed guidance for the major categories of catalysts: (1) peptide/protein catalysts, (2) nucleic acid catalysts and (3) synthetic catalysts. Also, as explained above, Applicants have provided general and specific guidance for carrying out the substrate reloading involved in the present method. Accordingly, Applicants respectfully submit that the breadth of the claims is commensurate in scope with the scope of enablement provided by the specification. Moreover, the Examiner's conclusion improperly excludes the permissibility for routine experimentation. See *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The Examiner also contends that "the state of the prior art at the time of the invention was made is such that each type of catalyst requires different reaction conditions (e.g., catalytic activity) and produces different product. In general the synthesis of libraries of catalysts do not have standard method and testing for their reactivities are known to be difficult."

The assertion that each type of catalyst requires different reaction conditions is not correct. As previously discussed, in a preferred embodiment, the method can be carried out under identical conditions. For example, as previously discussed, a library of protease catalysts can be compared under identical conditions. Moreover, as previously stated, this rejection is also seemingly the opposite of a rejection asserted by the prior Examiner, namely, that the assertion that the claims were limited to the situation in which all of the catalysts catalyze the same reaction and that all of the substrates react to form the same product. See the Office Action of April 23, 2002. In response, Applicants explained that the claims are not limited to the same catalytic reaction. Indeed, the claimed method is also applicable to catalysts that have the same or closely related catalytic activities (such as, a variant protease library) or to catalyst that have different catalytic activities. (See, e.g., original claims 9 and 10.)

In regard to the Examiner's assertion that "the synthesis of libraries of catalysts do not have standard method and testing for their reactivities are known to be difficult: (1) Applicants respectfully submit that the ability to synthesize of libraries of catalysts is routine in the art and (2) Applicants respectfully submit that assays used to determine catalytic activity are also well-known in the art and routine for the artisan.

Moreover, Applicants respectfully request the Examiner to provide evidence to support the conclusion that the synthesis of libraries of catalysts do not have standard method and testing for their reactivities and are known to be difficult.

The Examiner further contends that the art is inherently unpredictable because each type of catalyst has different catalytic activity and to select the catalyst with the desired catalytic activity of interest wherein the resulting mixture of catalyst is the same as the starting mixture of catalyst. This rejection is appears to be identical or very similar to the final basis given by the Examiner under conclusion a (above), and which was previously address. Again, Applicants respectfully direct the Examiner to the specification at page 10, line 14 to page 13, line 22, and the Examples, including Examples 4 and 8, which provides detailed guidance for how a catalyst of interest can be selected.

For the foregoing reasons, Applicants submit that the claims overcome the rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 28-33, 35-39, 48-53 and 55 under 35 U.S.C. 112, Indefiniteness

Claims 28-33, 35-39, 48-53 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

a. The Examiner contends that clarification is needed to the distinction being considered as "different" (e.g., type of catalyst, type of substrate, addition of a linker or carrier system) in the term "different unit" of claim 28.

Claim 28 has been amended to recite "providing a library of catalysts comprising at least two different catalysts present in the library as individual units having the structure catalyst-substrate." Applicants respectfully request reconsideration and withdrawal of this rejection.

b. The Examiner contends that claim 28 is vague and indefinite because it is unclear as to which of the two different units is being regenerated. The claims specifically recite that the catalyst-substrate units are regenerated. It is not clear what language the Examiner finds indefinite, and if the rejection is maintained, clarification is respectfully requested.

c. The Examiner contends that the term "conditions suitable" is a relative term which renders the claim indefinite. Applicants agree that the term "conditions suitable is a relative term", as it depends on what catalysts is being applied to the claimed method. Applicants disagree, however, that the term renders the claims indefinite. Indeed, the issue of indefiniteness is not based on whether a term is a relative term, but on whether a term would be understood by the artisan. Clearly, an artisan would understand that the term "conditions suitable" refers to the conditions suitable for the catalyst to catalyze the reaction of the at least one substrate to form one or more products. Indeed, this language is specifically recited in the claim itself.

d. The Examiner contends that the it is not clear in step (c) what the metes and bounds of the reagent or condition is being considered to convert the product to the substrate (e.g., the same reagent or condition is used to catalyst the substrate to the product.)

As would be understood by the artisan, many different conditions can be used to convert a substrate to a product and product to a substrate, as the claims are applicable to many different types of catalysts and substrates. In this regard, the specification provides many examples, including, enzymes, chemicals, pH, and temperature, as described, for example, in the specification at page 20 to page 22 and Examples 1-9.

e. The Examiner also requests clarification as to the link between the step of converting the product back to the substrate and the step of selecting the catalyst by immobilizing the product in claim 50.

Claim 50, depends from claim 29, which in turn depends from claim 28. Claim 50 recites "wherein said selecting step is performed by immobilizing said product molecule" and claim 29 specifies that the catalyst in claim 28 is "biologically amplifiable." Accordingly, claim 50 refers to a method of selecting a biologically amplifiable catalyst by the process of immobilization. For example, as described in the specification on page 33, an active catalyst can be selected over inactive catalyst by immobilization, including (i) the active catalysts can be isolated by immobilization of the product on a product binding column (or more generally, by means of the attached product). The product specific columns may immobilize the product through binding to a receptor molecule with specificity for the product, alternatively, immobilization may be mediated by a product-specific reaction between functional groups on the column and the product attached to the catalyst.

Thus, the link between (c) and the immobilization selection step (e) of claim 50 is that after step (c) is repeated at least once, the catalyst of interest is selected by an immobilization of the product produced by the catalyst of interest.

Applicants respectfully request withdrawal of this indefiniteness rejection.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. The Rejection of Claims 28-33, 35-39, 48-53 and 55 under 35 U.S.C. 112

Claims 28-33, 35-39, 48-53 and 55 are rejected under 35 U.S.C. 112, as omitting an essential step. The Examiner states that the omitted steps are the link between the step of converting the product back to substrate and the step of selecting a catalyst of interest.

This rejection is respectfully traversed. It is unclear what essential step the Examiner believes is missing. The claims recite a method for selecting a catalyst based on multiple catalytic turnovers, which is recited in steps (a) to (e). In particular, after multiple catalytic reactions according to the present invention, steps (a)-(d), a catalyst of interest is selected, step (e). Thus, the claims recite all of the essential steps necessary for carrying out the claimed invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 50-53 and 55 under 35 U.S.C. 112

Claims 50-53 and 55 are rejected under 35 U.S.C. 112, as allegedly lacking proper antecedent basis for the recitation "selecting step."

The recitation "selecting step" refers to the selecting recited in the step (e). In order to expedite prosecution, Applicants have removed the term "step."

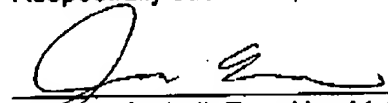
For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: December 5, 2003



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